Local Delivery of Rejuvenated Old Muscle Stem Cells to Increase Strength in Aged Patients

Grant Award Details

Local Delivery of Rejuvenated Old Muscle Stem Cells to Increase Strength in Aged Patients

Grant Type: Early Translational III

Grant Number: TR3-05501

Project Objective: The objective of this DCF project is to attain proof-of-concept that human muscle stem cells can be expanded ex vivo and used to treat female stress urinary incontinence (SUI) by injection into the urinary sphincter in a rodent model of SUI.

Investigator:

Name:	Helen Blau
Institution:	Stanford University
Type:	PI

Disease Focus: Aging, Skeletal/Smooth Muscle disorders

Human Stem Cell Use: Adult Stem Cell

Award Value: $1,825,920

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: NCE Progress Report

View Report

Grant Application Details

Application Title: Local Delivery of Rejuvenated Old Muscle Stem Cells to Increase Strength in Aged Patients

Public Abstract: As humans age, the ability to regenerate skeletal muscle tissue is impaired. Injuries to the musculoskeletal system that require extended periods of immobilization lead to muscle atrophy and are particularly devastating to the elderly population. Loss of skeletal muscle mass and function reduces mobility, which negatively affects quality of life, and increases the risk of mobility-related accidents. Currently, strategies to ameliorate injury-related or heritable muscle atrophy are limited and consist primarily of exercise-based regimens to increase strength. Here we propose to develop a human stem cell therapy to prevent and/or reverse localized skeletal muscle atrophy in muscles of the aged. Specifically, we aim to (1) refine a strategy we have developed that enables us to isolate muscle stem cells (MuSCs) from human muscle biopsies, (2) apply a strategy which we developed for murine MuSCs to human MuSCs that rejuvenates and expands the stem cells in culture to clinically useful numbers using a combined bioengineering and small molecule treatment, and (3) demonstrate that transplantation of human MuSCs results in increased in vivo force generation and strength in atrophied muscles of aged recipients. Together, these studies will culminate in the validation of a novel stem cell-based "development candidate" to the treat skeletal muscle atrophy afflicting the ever increasing aged community and will advance the use of stem cells for therapy in the clinic.

Statement of Benefit to California: Skeletal muscle is critical to our day-to-day movement and loss of muscle mass and function impairs quality of life and increases the risk of mobility related accidents particularly in the elderly. Currently there are no clinical approaches to prevent or reverse the muscle atrophy that occurs following musculoskeletal injury and subsequent immobilization other than physical activity. Since California is projected to be the fastest growing state in the U.S. in terms of population, with an elderly population that is projected to grow twice as fast as the total population of the state, it is more important than ever to develop strategies that positively impact the health of this demographic. The research in this CIRM application aims to provide a muscle stem cell transplantation therapy to overcome muscle atrophy. Initially, the application of this strategy to the function of small muscles of the eye critical to vision, to the pharynx critical to swallowing, or to the muscles of the hand are envisioned. A major effort will also entail scaling up muscle stem cell production for the treatment muscle atrophy occurring in ~60% of the aged knee or hip revision rehabilitation patients. This work will not only advance the use of stem cells in the clinic, but will also provide a novel therapy to ameliorate the devastating effects of muscle atrophy in our ever growing aged community.